

## REMARKS

Upon entry of the proposed amendment, claims 1-47 are pending.

### 35 U.S.C. § 103

Claims 1-19, 20-35, and 36-47 stand rejected under 35 U.S.C. §103(a) as being obvious over US Patent No. 6,399,793 (Kronenthal et al). Applicants respectfully submit that the Examiner's position is not well based.

To establish a prima facie case of obviousness, there must be some suggestion or incentive that would have motivated the skilled artisan to modify a reference. *See* MPEP 2142; *Karsten Mfg. Corp. v. Cleveland Gulf Co.*, 242 F.3d 1376, 1385 (Fed. Cir. 2001). Moreover, the proposed modification of the prior art must have had a reasonable expectation of success. *See* MPEP 2142; *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209 (Fed. Cir. 1991).

The Kronenthal reference only discloses that an aryl ester reacts with a sulfur ylide to produce a keto ylide, which is subsequently converted to an alpha-chloroketone. Nowhere in the Kronenthal reference mentions or even suggests that an alkyl ester can also react with a sulfur ylide. It is well recognized by those skilled in the chemistry art that the chemical behavior of an aryl ester is qualitatively different from an alkyl ester. A contemporary chemistry textbook describes the situation as follows:

Another factor which strongly affects the reactivity of these carboxylic acid derivatives is the leaving-group ability of the substituents. The order is  $\text{Cl} > \text{OAr} > \text{OR}$  . . . so that not only does the ease of forming the tetrahedral intermediate decrease in the order  $\text{Cl} > \text{OAr} > \text{OR}$  . . . , but the tendency for subsequent elimination to occur is also in the same order. Because the two factors work together, there are large differences in reactivity toward the nucleophiles.

*See* Carey & Sundberg, "Advanced Organic Chemistry, Part A: Structure and Mechanisms," page 473 (Fourth Edition, 2000). Thus, the prior art cited by the Examiner lacks the requisite suggestion or motivation to use a less reactive alkyl ester in replacement of an aryl ester in the present invention.

Additionally, Elias J. Corey, a Nobel Laureate who first reported the sulfur ylide reagent, observed that "[d]imethylsulfoxonium methylide (I) can be acylated by treatment

with reactive carboxylic acid derivatives such as acid chlorides and phenyl esters to give stable  $\beta$ -ketosulfoxonium ylides." *See* J. Am. Chem. Soc., 86, 1640 (1964). It is evident that, based on his understanding of the  $\text{Cl} > \text{OAr} > \text{OR}$  reactivity relationship, Corey was excluding alkyl esters in the reaction with dimethylsulfoxonium ylide. In fact, Corey further expressly stated that ethyl esters did not react with the same dimethylsulfoxonium ylide, *see id.*, and no counter point of view appeared in the literature for the next 40 years except for the case of highly reactive fluorinated esters which Applicants point out in the present application. Therefore, this prior art teaches away from the present invention, and it is well established that a teaching away from the proposed modification represents "strong evidence of unobviousness." *See In re Hedges*, 783 F.2d 1038, 1041 (Fed. Cir. 1986).

Accordingly, the Applicants' invention is not obvious over the Kronenthal reference because the prior art not only lacks the requisite suggestion or motivation, but also teaches away from the instant invention. Applicants respectfully request withdrawal of the 35 U.S.C. § 103 rejection.

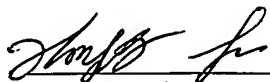
### 35 U.S.C. § 112

Claims 48-50 stand rejected under 35 U.S.C. § 112 as being indefinite. Applicants have cancelled claims 48-50, and thus making this rejection moot.

In view of the amendments and remarks, Applicants respectfully submit that the application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

Bristol-Myers Squibb Company  
Patent Department  
P.O. Box 4000  
Princeton, NJ 08543-4000  
(609) 252-6457  
Date: October 28, 2004

  
Henry H. Gu  
Agent for Applicants  
Reg. No. 55,227